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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/738,455	12/16/2003	Timothy J. Jegla	018512-001420US	9589

20350 7590 01/12/2007
TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/738,455	JEGLA, TIMOTHY J.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-15* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 16-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *11-15* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/6/03*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *included*.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Appendix A*.

DETAILED ACTION

1. This office action is response to Applicant's election of Group II, claims 11-15, drawn to isolated potassium channel polypeptide. Election was made with traverse in the response filed 10/20/2006. The traversal is on the ground(s) that the search of all claims would not impose a serious burden on the Office because Applicant alleges that all the groups stem from a common concept and theory. This is not found to be persuasive because the restriction was done under U.S. practice (35 U.S.C. 111(a)) thus the argument regarding common concept and theory is misplaced. However, even under PCT Rule 13.2, the claims lack the same or corresponding special technical features for the following reasons: each group is directed to different compounds and/or methods (Applicant argued this in the parent case 09/719919) and the claims are not so linked by a special technical feature within the meaning of PCT Rule 13.2 so as to form a single inventive concept. Thus, it is proper to separate the various composition and the methods claims. The Office in the restriction requirement mailed 9/21/2006 established that Inventions I-VIII in the instant application are independent or distinct requiring different classification and different field of search. It also established there would be serious search burden. In addition, in the absence of a common core sequence, searching more than one sequence would result in undue search burden on the Office. Therefore, the restriction requirement is deemed proper and made FINAL. Claims 1-10 and 16-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or

linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/20/2006.

Further, Applicant had elected the nucleotide sequence of SEQ ID NO: 18. Since, the claims are drawn to the polypeptide, the Office contacted Ms. Annette Parent (Applicant's representative) and clarified the sequence selection for examination (see interview summary). The Office as thus searched polypeptide of SEQ ID NO: 17 for examination purposes.

Specification

2. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

3. The use of the trademark Transfectam and Lipofectin (p.53) etc. has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see p. 23). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Priority

5. Applicant claims benefit to provisional application 60/091, 466, filed 07/01/1998. However, this application does not contain a sequence of SEQ ID NO: 17 that is 519 amino acids long (human) but only contains SEQ ID NO: 1 that is 506 amino acids long (mouse). SEQ ID NO: 17 was first disclosed in PCT/US99/14945. Therefore, Applicant is entitled to a priority date of 6/30/1999 (filing date of PCT/US99/14945) with respect to SEQ ID NO: 17, because application PCT/US99/14945 discloses SEQ ID NO: 17 that is 519 amino acids long.

6. Applicant is required to update the priority information by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Information Disclosure Statement

7. The information disclosure statement (IDS) submitted on 12/06/2003 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner is considering the information disclosure statement. The Office has added the journal information to the Zhu et al. reference.

Claim Objections

8. Claims 11, 14 and 15 are objected to because they recite multiple inventions (including those non-elected). Applicant is required to amend the claims to recite only the elected invention, specifically to the elected polypeptide sequence.

8a. Claim 11 is objected to because there are three subparts to the claim, which are numbered (i), (ii) and (iv). Applicant is required to correct the numbering information.

Claim Rejections - 35 USC § 112, second paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9a. Claims 11-13 and 15 are rejected as being vague and indefinite in the recitation of the term "Kv alpha subunit or Kv6.2". Abbreviations and acronyms should be spelled out at their first use in the claims for clarity. The protein of interest is described by an arbitrary abbreviation. Claiming biochemical molecules by a particular abbreviated name given to the protein by various workers in the field fails to distinctly claim what that protein is. Claim 14 is rejected insofar as they depend from claim 11.

Claim Rejections - 35 USC § 112, first paragraph

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10a. Claims 11-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses the polypeptide of SEQ ID NO: 1 or SEQ ID NO: 17. This meets the written description provisions of 35 USC 112, first paragraph. However, the specification does not disclose all polypeptide monomers comprising an alpha subunit of a heteromeric potassium channel, the polypeptide monomer: having the ability to form, with at least one additional Kv alpha subunit, a heteromeric potassium channel or having a monomer subunit association region that has greater than about 70% amino acid sequence identity to a Kv6.2 subunit association region or specifically binding to polyclonal antibodies generated against SEQ ID NO: 1 or SEQ ID NO: 17 or having an S4-S6 region that has greater than about 85% amino acid sequence identity to a Kv6.2 S4-S6 region. The claims also recite the phrases "an amino acid sequence" and thus, are broadly interpreted by the Examiner as reading upon: (i) protein variants with any number of deletions, substitutions, or additions and (ii) fragments of SEQ ID NOs: 1 or 17 or human Kv6.2 or mouse Kv6.2, including sequences only 25 amino acids in length (see specification pages 21 and 50). The claims as written, however, encompass polypeptide sequences which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 11-15. The specification does not provide adequate written description to support the genus encompassed by the instant claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*See Vas-Cath* at page 1116).

With the exception of the polypeptide of SEQ ID NO: 1 or SEQ ID NO: 17, the skilled artisan cannot envision all the detailed chemical structure of the claimed nucleic acid sequences, regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only the polypeptide of SEQ ID NO: 1 or SEQ ID NO: 17, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. As a result, it does not appear that the inventors were in possession of various polypeptide sequences set forth in claims 11-15.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

10b. Claims 11-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein comprising the amino acid sequence of SEQ ID NO: 1 or SEQ ID NO: 17, does not reasonably provide enablement for all

polypeptide monomers comprising an alpha subunit of a heteromeric potassium channel, the polypeptide monomer: having the ability to form, with at least one additional Kv alpha subunit, a heteromeric potassium channel or having a monomer subunit association region that has greater than about 70% amino acid sequence identity to a Kv6.2 subunit association region or specifically binding to polyclonal antibodies generated against SEQ ID NO: 1 or SEQ ID NO: 17 or having an S4-S6 region that has greater than about 85% amino acid sequence identity to a Kv6.2 S4-S6 region. The claims also recite the phrases "an amino acid sequence" and thus, are broadly interpreted by the Examiner as reading upon: (i) protein variants with any number of deletions, substitutions, or additions and (ii) fragments of SEQ ID NOs: 1 or 17 or human Kv6.2 or mouse Kv6.2, including sequences only 25 amino acids in length (see specification pages 21 and 50). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the

existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The instant claims read on all polypeptide monomers comprising an alpha subunit of a heteromeric potassium channel, the polypeptide monomer: having the ability to form, with at least one additional Kv alpha subunit, a heteromeric potassium channel or having a monomer subunit association region that has greater than about 70% amino acid sequence identity to a Kv6.2 subunit association region or specifically binding to polyclonal antibodies generated against SEQ ID NO: 1 or SEQ ID NO: 17 or having an S4-S6 region that has greater than about 85% amino acid sequence identity to a Kv6.2 S4-S6 region. The claims also recite the phrases "an amino acid sequence" and thus, are broadly interpreted by the Examiner as reading upon: (i) protein variants with any number of deletions, substitutions, or additions and (ii) fragments of SEQ ID NOs: 1 or 17 or human Kv6.2 or mouse Kv6.2, including sequences only 25 amino acids in length (see specification pages 21 and 50).

However, other than the polypeptide of SEQ ID NO: 1 or 17, the specification as filed fails to disclose any other polypeptide sequences. Despite knowledge in the art for producing variants of a given protein with amino deletions, insertions or substitutions the specification fails to provide any guidance regarding the changes/modifications contemplated and yet retain the function of the protein. Furthermore, detailed information regarding the structural and functional requirements of the disclosed protein is lacking. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in

binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990; Ngo et al., 1994). Although it is accepted that the amino acid sequence of a polypeptide determines its structural and functional properties, predicting a protein's structure and function from mere sequence data remains an elusive task. Therefore, predicting which variants of the protein would retain the functions of the protein is well outside the realm of routine experimentation. Thus, undue amount of experimentation would be required to generate changes/modifications contemplated and yet retain the function of the proteins claimed.

Applicants have not taught how one of skill in the art would use the full scope of polypeptide sequences encompassed by the invention of claims 11-15. The specification as filed does not sufficiently teach one of skill in the art how to make and/or use the full scope of the claimed sequences. The amount of experimentation required to make and/or use the full scope of the claimed sequences would require trial and error experimentation to determine the functional sequences. Given the breadth of claims 11-15, in light of the unpredictability of the art as determined by the lack of working examples and shown by the prior at of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11a. Claims 12-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Su et al. (1997).

Claims are drawn to all polypeptide monomers comprising an alpha subunit of a heteromeric potassium channel, the polypeptide monomer: having the ability to form, with at least one additional Kv alpha subunit, a heteromeric potassium channel or having a monomer subunit association region that has greater than about 70% amino acid sequence identity to a Kv6.2 subunit association region or specifically binding to polyclonal antibodies generated against SEQ ID NO: 1 or SEQ ID NO: 17 or having an S4-S6 region that has greater than about 85% amino acid sequence identity to a Kv6.2 S4-S6 region. The claims also recite the phrases "an amino acid sequence" and thus, are broadly interpreted by the Examiner as reading upon: (i) protein variants with any number of deletions, substitutions, or additions and (ii) fragments of SEQ ID NOs: 1 or 17 or human Kv6.2 or mouse Kv6.2, including sequences only 25 amino acids in length (see specification pages 21 and 50).

Su et al. et al. disclose an amino acid sequence that has 53.7% over all identity to SEQ ID NO: 17 of the instant invention (see Appendix A1-5, page 678). The reference also discloses a region with at least 25 amino acids identical to the instant

invention. Su et al. indicate that although no voltage-dependent K^+ current was detected in the oocytes microinjected with KH2 cRNA, it is possible that KH2 form functional heterotetrameric channels with other potassium genes (p.680). Therefore, claims 12-14 are rejected as being anticipated by Su et al. (1997).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12a. Claims 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Su et al. (1997) in view of Jacobs et al. (U.S. Patent No: 5 965 397).

Claims are drawn to all polypeptide monomers comprising an alpha subunit of a heteromeric potassium channel, the polypeptide monomer: having the ability to form, with at least one additional Kv alpha subunit, a heteromeric potassium channel or

having a monomer subunit association region that has greater than about 70% amino acid sequence identity to a Kv6.2 subunit association region or specifically binding to polyclonal antibodies generated against SEQ ID NO: 1 or SEQ ID NO: 17 or having an S4-S6 region that has greater than about 85% amino acid sequence identity to a Kv6.2 S4-S6 region. The claims also recite the phrases "an amino acid sequence" and thus, are broadly interpreted by the Examiner as reading upon: (i) protein variants with any number of deletions, substitutions, or additions and (ii) fragments of SEQ ID NOs: 1 or 17 or human Kv6.2 or mouse Kv6.2, including sequences only 25 amino acids in length (see specification pages 21 and 50).

The teachings of Su et al. are. disclosed above in 11a. However, Su et al. disclosure does not teach polyclonal antibodies that bind to polypeptide of SEQ ID NO: 17.

Jacobs et al. et al. describes the generation of polyclonal antibodies capable of binding a protein (column 41, lines 50-60). Therefore, it would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to generate polyclonal antibodies as taught by Jacobs et al. using the polypeptide described in Su et al. (that has an overall identity of 53 % to SEQ ID NO: 17, see Appendix A1-5). The person of ordinary skill in the art would have been motivated to generate monoclonal antibodies directed to the polypeptide described by Su et al. because this will allow one of skilled in the art to use the antibodies for immunodetection or therapeutic or diagnostic purposes. There is a reasonable expectation of success because generating various antibodies to specific proteins for purification, expression

studies and therapeutic purposes is routine in the art. Therefore, the claims 11-15 are rejected as obvious over Su et al. (1997) in view of Jacobs et al. (U.S. Patent No: 5 965 397).

Relevant Prior Art

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Ottschytsch, N. et al. Obligatory heterotetramerization of three previously uncharacterized Kv channel alpha-subunits identified in the human genome, (June, 2002), PNAS, Vol.99, NO: 12, pp7986-7991. Describes various Kv channel sequences. Capable of encoding a protein, which has 99.3% sequence homology to SEQ ID NO: 17. However, this was published after the earliest filing date.

Conclusion

14. No claims are allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JS
Art Unit 1647,
January 2, 2007

Sesathason Sekoratayan
Patent Examiner

Appendix A2 : Applicant's copy

```
RA   Clegg S., Cobley V.E., Collier R.E., Connor R.E., Corby N.R.,
RA   Coulson A., Coville G.J., Deadman R., Dhami P.D., Dunn M.,
RA   Ellington A.G., Frankland J.A., Fraser A., French L., Garner P.,
RA   Grafham D.V., Griffiths C., Griffiths M.N.D., Gwilliam R., Hall R.E.,
RA   Hammond S., Harley J.L., Heath P.D., Ho S., Holden J.L., Howden P.J.,
RA   Huckle E., Hunt A.R., Hunt S.E., Jekosch K., Johnson C.M., Johnson D.,
RA   Kay M.P., Kimberley A.M., King A., Knights A., Laird G.K., Lawlor S.,
RA   Lehvaeslaiho M.H., Leversha M.A., Lloyd C., Lloyd D.M., Lovell J.D.,
RA   Marsh V.L., Martin S.L., McConnachie L.J., McLay K., McMurray A.A.,
RA   Milne S.A., Mistry D., Moore M.J.F., Mullikin J.C., Nickerson T.,
RA   Oliver K., Parker A., Patel R., Pearce T.A.V., Peck A.I.,
RA   Phillimore B.J.C.T., Prathalingam S.R., Plumb R.W., Ramsay H.,
RA   Rice C.M., Ross M.T., Scott C.E., Sehra H.K., Shownkeen R., Sims S.,
RA   Skuce C.D., Smith M.L., Soderlund C., Steward C.A., Sulston J.E.,
RA   Swann R.M., Sycamore N., Taylor R., Tee L., Thomas D.W., Thorpe A.,
RA   Tracey A., Tromans A.C., Vaudin M., Wall M., Wallis J.M.,
RA   Whitehead S.L., Whittaker P., Willey D.L., Williams L., Williams S.A.,
RA   Wilming L., Wray P.W., Hubbard T., Durbin R.M., Bentley D.R., Beck S.,
RA   Rogers J.;
RT   "The DNA sequence and comparative analysis of human chromosome 20.";
RL   Nature 414:865-871(2001).
RN   [3]
RP   NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORM 2).
RC   TISSUE=Muscle;
RX   MEDLINE=22388257; PubMed=12477932; DOI=10.1073/pnas.242603899;
RA   Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA   Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA   Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
RA   Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA   Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA   Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA   Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA   Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA   Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA   Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA   Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA   Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
RA   Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA   Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA   Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
RA   Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
RA   Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
RT   "Generation and initial analysis of more than 15,000 full-length human
RT   and mouse cDNA sequences.";
RL   Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
CC   -!- FUNCTION: Probable potassium channel subunit. May need to
CC       associate with another protein to form a functional channel. May
CC       modulate channel activity.
CC   -!- SUBUNIT: Heterotetramer of potassium channel proteins (By
CC       similarity).
CC   -!- SUBCELLULAR LOCATION: Membrane; multi-pass membrane protein.
CC   -!- ALTERNATIVE PRODUCTS:
CC       Event=Alternative splicing; Named isoforms=2;
CC       Name=1;
CC         IsoId=Q9UIX4-1; Sequence=Displayed;
CC       Name=2;
CC         IsoId=Q9UIX4-2; Sequence=VSP_001024, VSP_001025;
CC         Note=No experimental confirmation available;
CC   -!- TISSUE SPECIFICITY: Detected in brain and placenta, and at much
CC       lower levels in kidney and pancreas.
CC   -!- DOMAIN: The segment S4 is probably the voltage-sensor and is
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Appendix A3 Applicant's copy

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CC       characterized by a series of positively charged amino acids at
CC       every third position.
CC   -!- SIMILARITY: Belongs to the potassium channel family. G subfamily.
CC   ---------------------------------------------------------------------
CC   Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
CC   Distributed under the Creative Commons Attribution-NoDerivs License
CC   ---------------------------------------------------------------------
DR   EMBL; AF033383; AAC05635.1; -; mRNA.
DR   EMBL; AL050404; CAB51753.1; -; Genomic_DNA.
DR   EMBL; BC006367; AAH06367.1; -; mRNA.
DR   PIR; JC5920; JC5920.
DR   HSSP; Q16968; 1EOE.
DR   Ensembl; ENSG00000026559; Homo sapiens.
DR   HGNC; HGNC:6248; KCNG1.
DR   MIM; 603788; gene.
DR   GO; GO:0016021; C:integral to membrane; NAS.
DR   GO; GO:0005267; F:potassium channel activity; NAS.
DR   GO; GO:0006813; P:potassium ion transport; NAS.
DR   InterPro; IPR000210; BTB.
DR   InterPro; IPR005821; Ion_trans.
DR   InterPro; IPR001622; K+channel_pore.
DR   InterPro; IPR003091; K_channel.
DR   InterPro; IPR003131; K_tetra.
DR   InterPro; IPR003969; Kv6_channel.
DR   InterPro; IPR003968; Kv_channel.
DR   InterPro; IPR005820; M+channel_nlg.
DR   Pfam; PF00520; Ion_trans; 1.
DR   Pfam; PF02214; K_tetra; 1.
DR   PRINTS; PR00169; KCHANNEL.
DR   PRINTS; PR01492; KV6CHANNEL.
DR   PRINTS; PR01491; KVCHANNEL.
DR   SMART; SM00225; BTB; 1.
KW   Alternative splicing; Ion transport; Ionic channel; Membrane;
KW   Potassium; Potassium channel; Potassium transport; Transmembrane;
KW   Transport; Voltage-gated channel.
FT   CHAIN         1    513       Potassium voltage-gated channel subfamily
FT                                G member 1.
FT                                /FTId=PRO_0000054073.
FT   TOPO_DOM      1    227       Cytoplasmic (Potential).
FT   TRANSMEM    228    248       Segment S1 (Potential).
```

start | next page

Appendix A 4 Applicant's copy

SCORE Search Results Details for Application 10738455 and Search Result $itemName.

Score Home Page | Retrieve Application List | SCORE System Overview | SCORE FAQ | Comments / Suggestions

This page gives you Search Results detail for the Application 10738455 and Search Result $itemName.

start

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                          FT   TRANSMEM    268    288       Segment S2 (Potential).
FT   TOPO_DOM     289     302       Cytoplasmic (Potential).
FT   TRANSMEM     303     323       Segment S3 (Potential).
FT   TRANSMEM     343     363       Segment S4 (Potential).
FT   TOPO_DOM     364     376       Cytoplasmic (Potential).
FT   TRANSMEM     377     397       Segment S5 (Potential).
FT   TRANSMEM     440     460       Segment S6 (Potential).
FT   TOPO_DOM     461     513       Cytoplasmic (Potential).
FT   REGION       412     432       Segment H5 (pore-forming) (Potential).
FT   MOTIF        424     429       Selectivity filter (By similarity).
FT   COMPBIAS      61      64       Poly-Arg.
FT   COMPBIAS     254     257       Poly-Glu.
FT   VARSPLIC     259     275       GHCSQMCHNVFIVESVC -> VRAHAPRGNAPPRGKGL
FT                                  (in isoform 2).
FT                                  /FTId=VSP_001024.
FT   VARSPLIC     276     513       Missing (in isoform 2).
FT                                  /FTId=VSP_001025.
FT   CONFLICT     426     426       G -> D (in Ref. 1).
FT   CONFLICT     465     465       R -> P (in Ref. 1).
SQ   SEQUENCE   513 AA;  57913 MW;  A002F1C0EF2FBDC5 CRC64;

  Query Match             53.7%;  Score 1449;  DB 1;  Length 513;
  Best Local Similarity   60.1%;  Pred. No. 2e-106;
  Matches  286;  Conservative   63;  Mismatches  105;  Indels   22;  Gaps    5;

Qy          15 HHYGSHSPWSQLLSSPMETP---SIKGLYYRRVRKVGALD-----ASPVDLKKEILINVG 66
               : | : |  |      |   |   :||| :||| :::   |       | | :: |:||||
Db          11 YDYSALSCTSDASFHPAFLPQRQAIKGAFYRRAQRLRPQDEPRQGCQPEDRRRRIIINVG 70

Qy          67 GRRYLLPWSTLDRFPLSRLSKLRLCRSYEEIVQLCDDYDEDSQEFFFDRSPSAFGVIVSF 126
               | :| |||:||| |||:|| :|: | ::::|: :|||||    ||||||:| ||| |::|
Db          71 GIKYSLPWTTLDEFPLTRLGQLKACTNFDDILNVCDDYDVTCNEFFFDRNPGAFGTILTF 130

Qy         127 LAAGKLVLLQEMCALSFQEELAYWGIEEAHLERCCLRKLLRKLEELEELAKLHRED--VL 184
               | |||| ||:|||||||||||| |||| | ||: || |: |:|:||  |: :   ||  :
Db         131 LRAGKLRLLREMCALSFQEELLYWGIAEDHLDGCCKRRYLQKIEEFAEMVEREEEDDALD 190

Qy         185 RQQRETRRPASHSSRWGLCMNRLREMVENPQSGLPGKVFACLSILFVATTAVSLCVSTMP 244
                : |::  ||    | | || |||:|||. | |||||||||||:|||  |||:| |||:|
Db         191 SEGRDSEGPAEGEGRLGRCMRRLRDMVERPHSGLPGKVFACLSVLFVTVTAVNLSVSTLP 250

Qy         245 DLRAEEDQGECSRKCYYIFIVETICVAWFSLEFCLRFVQAQDKCQFFQGPLNIIDILAIS 304
               || ||:|| ||: |: :||||::|| |||||| || :|| |  | : || :||::||
Db         251 SLREEEEQGHCSQMCHNVFIVESVCVGWFSLEFLLRLIQAPSKFAFLRSPLTLIDLVAIL 310

Qy         305 PYYVSLAVSEEPPEDGERPSR------SSYLEKVGLVLRVLRALRILYVMRLARHSLGLQ 358
               |||::| |      ||    |      :|||:||||||||||||||||||||||||||
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Appendix A-5 Applicant's copy

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Db        311 PYYITLLV------DGAAAGRRKPGAGNSYLDKVGLVLRVLRALRILYVMRLARHSLGLQ 364

Qy        359 TLGLTVRRCTCEFGLLLLFLAVAITLFSPLVYVAEKESGRVLEFTSIPASYWWAIISMTT 418
              ||||| |||| ||||||||| ||| ||:||:|| | |     ||||||| ||||:|:|||
Db        365 TLGLTARRCTREFGLLLLFLCVAIALFAPLLYVIENEMADSPEFTSIPACYWWAVITMTT 424

Qy        419 VGYGDMVPRSVPGQMVALSSILSGILIMAFPATSIFHTFSHSYLELKKEQEQLQAR 474
              |||||||||| |||:|||||||||||:|||| |||||||| ||||||:|||::  |
Db        425 VGYGDMVPRSTPGQVVALSSILSGILLMAFPVTSIFHTFSRSYLELKQEQERVMFR 480


RESULT 9
Q4S656_TETNG
ID   Q4S656_TETNG   PRELIMINARY;   PRT;   518 AA.
AC   Q4S656;
DT   19-JUL-2005, integrated into UniProtKB/TrEMBL.
DT   19-JUL-2005, sequence version 1.
DT   07-FEB-2006, entry version 6.
DE   Chromosome 9 SCAF14729, whole genome shotgun sequence.
GN   ORFNames=GSTENG00023439001;
OS   Tetraodon nigroviridis (Green puffer).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;
OC   Acanthomorpha; Acanthopterygii; Percomorpha; Tetraodontiformes;
OC   Tetradontoidea; Tetraodontidae; Tetraodon.
OX   NCBI_TaxID=99883;
RN   [1]
RP   NUCLEOTIDE SEQUENCE.
RX   PubMed=15496914; DOI=10.1038/nature03025;
RA   Jaillon O., Aury J.-M., Brunet F., Petit J.-L., Stange-Thomann N.,
RA   Mauceli E., Bouneau L., Fischer C., Ozouf-Costaz C., Bernot A.,
RA   Nicaud S., Jaffe D., Fisher S., Lutfalla G., Dossat C., Segurens B.,
RA   Dasilva C., Salanoubat M., Levy M., Boudet N., Castellano S.,
RA   Anthouard V., Jubin C., Castelli V., Katinka M., Vacherie B.,
RA   Biemont C., Skalli Z., Cattolico L., Poulain J., De Berardinis V.,
RA   Cruaud C., Duprat S., Brottier P., Coutanceau J.-P., Gouzy J.,
RA   Parra G., Lardier G., Chapple C., McKernan K.J., McEwan P., Bosak S.,
RA   Kellis M., Volff J.-N., Guigo R., Zody M.C., Mesirov J.,
RA   Lindblad-Toh K., Birren B., Nusbaum C., Kahn D., Robinson-Rechavi M.,
RA   Laudet V., Schachter V., Quetier F., Saurin W., Scarpelli C.,
RA   Wincker P., Lander E.S., Weissenbach J., Roest Crollius H.;
RT   "Genome duplication in the teleost fish Tetraodon nigroviridis reveals
RT   the early vertebrate proto-karyotype.";
RL   Nature 431:946-957(2004).
RN   [2]
RP   NUCLEOTIDE SEQUENCE.
RG   Genoscope; Whitehead Institute Centre for Genome Research;
RL   Submitted (FEB-2004) to the EMBL/GenBank/DDBJ databases.
CC   -!- CAUTION: The sequence shown here is derived from an
CC       EMBL/GenBank/DDBJ whole genome shotgun (WGS) entry which is
CC       preliminary data.
CC   ---------------------------------------------------------------------
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CC   Distributed under the Creative Commons Attribution-NoDerivs License
CC   ---------------------------------------------------------------------
DR   EMBL; CAAE01014729; CAG03876.1; -; Genomic_DNA.
DR   GO; GO:0016021; C:integral to membrane; IEA.
DR   GO; GO:0016020; C:membrane; IEA.
DR   GO; GO:0008076; C:voltage-gated potassium channel complex; IEA.
DR   GO; GO:0005249; F:voltage-gated potassium channel activity; IEA.
DR   GO; GO:0006812; P:cation transport; IEA.
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Appendix A Applicant's copy

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Qy          96 EIVQLCDDYDEDSQEFFFDRSPSAFGVIVSFLAAGKLVLLQEMCALSFQEELAYWGIEEA 155
               ||: :|||||    |:|||||||||  ||:|||||| ||:||||||||||| |||:||
Db          61 EIMDVCDDYDGSRNEYFFDRSPSAFRTIVTFLAAGKLRLLREMCALSFQEELLYWGVEEN 120

Qy         156 HLERCCLRKLLRKLEELEELAKLHREDVLRQQRETRRPAS------------HSSRWGL 202
               :|: ||||||  : || :|  :|  ||      |   | |                :|
Db         121 NLDWCCLRKLRLRQEEYKEQQRLEEEDT-----ELTSPQSCEENLQPLDVGLQEDTRSAG 175

Qy         203 CMNRLREMVENPQSGLPGKVFACLSILFVATTAVSLCVSTMPDLRAEEDQGECSRKCYYI 262
               || |||:|||||| ||||||:|||||:|||| |||:|||||||||| ||::||||::|: |
Db         176 CMGRLRDMVENPHSGLPGKIFACLSVLFVAITAVTLCVSTMPDLREEEERGECSQRCHNI 235

Qy         263 FIVETICVAWFSLEFCLRFVQAQDKCQFFQGPLNIIDILAISPYYVSLAVSEEPPEDGER 322
               ||:||:|| |||||| |||:| | || | : |||:||::|| |||::| |  :   || :
Db         236 FILETVCVGWFSLEFLLRFIQTQSKCTFLRTPLNVIDVVAILPYYITLIV--DSLSDGGK 293

Qy         323 P--SRSSYLEKVGLVLRVLRALRILYVMRLARHSLGLQTLGLTVRRCTCEFGLLLLFLAV 380
                 | ::||||||||||||||||| |||||||||||| |||||:||| |||||||| |.
Db         294 TAGSGNNYLEKVGLVLRVLRALRIFYVMRLARHSLGLQVLGLTVKRCTREFGLLLLFLCV 353

Qy         381 AITLFSPLVYVAEKESGRVLEFTSIPASYWWAIISMTTVGYGDMVPRSVPGQMVALSSIL 440
               |: ||||||::|| | |   |||||| |||||:||||||||||||||:|||:|||||||
Db         354 AMALFSPLVFLAESEMGAKQEFTSIPGSYWWAVISMTTVGYGDMVPRSIPGQVVALSSIL 413

Qy         441 SGILIMAFPATSIFHTFSHSYLELKKEQEQL 471
               ||||:|||| |||||||| ||||||:|| ::   .
Db         414 SGILLMAFPVTSIFHTFSRSYLELKEEQSRM 444
```

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RESULT 8
KCNG1_HUMAN
ID   KCNG1_HUMAN    STANDARD;      PRT;   513 AA.
AC   Q9UIX4; O43528; Q9BRC1;
DT   25-OCT-2002, integrated into UniProtKB/Swiss-Prot.
DT   01-MAY-2000, sequence version 1.
DT   07-MAR-2006, entry version 44.
DE   Potassium voltage-gated channel subfamily G member 1 (Voltage-gated
DE   potassium channel subunit Kv6.1) (kH2).
GN   Name=KCNG1;
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae;
OC   Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   NUCLEOTIDE SEQUENCE (ISOFORM 1).
RC   TISSUE=Fetal brain;
RX   MEDLINE=98096380; PubMed=9434767; DOI=10.1006/bbrc.1997.7830;
RA   Su K., Kyaw H., Fan P., Zeng Z., Shell B.K., Carter K.C., Li Y.;
RT   "Isolation, characterization, and mapping of two human potassium
RT   channels.";
RL   Biochem. Biophys. Res. Commun. 241:675-681(1997).
RN   [2]
RP   NUCLEOTIDE SEQUENCE [LARGE SCALE GENOMIC DNA].
RX   MEDLINE=21638749; PubMed=11780052; DOI=10.1038/414865a;
RA   Deloukas P., Matthews L.H., Ashurst J.L., Burton J., Gilbert J.G.R.,
RA   Jones M., Stavrides G., Almeida J.P., Babbage A.K., Bagguley C.L.,
RA   Bailey J., Barlow K.F., Bates K.N., Beard L.M., Beare D.M.,
RA   Beasley O.P., Bird C.P., Blakey S.E., Bridgeman A.M., Brown A.J.,
RA   Buck D., Burrill W.D., Butler A.P., Carder C., Carter N.P.,
RA   Chapman J.C., Clamp M., Clark G., Clark L.N., Clark S.Y., Clee C.M.,
```